(19) JAPANESE PATENT OFFICE

PATENT ABSTRACTS OF JAPAN

(11) Publication number: 03044324 A

(43) Date of publication of application: 26.02.91

(51) Int. Cl A61K 31/52
// C07D473/06

(21) Application number: 01180867

(22) Date of filing: 13.07.89

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(54) SEXUAL FUNCTION INVIGORATOR

(57) Abstract

PURPOSE: To obtain sexual function invigorator having excellent action stimulating hypothalamus or limbic system and invigorating sexual function containing propentofylline or intracorporeal metabolite of said propentofylline as active ingredient.

CONSTITUTION: The aimed sexual function invigorator contains propentofylline [namely, xantine derivative such as 3-methyl-1-(5-oxohexyl)-7-propyl-7H-purine-2(3 -H),6(1H)-dione] or intracorporeal metabolite of said compound (namely, 5- oxohexyl in the propentofylline is modified to 5-hydroxyhexyl, 4-carboxybutyl or 3-carboxypropyl) as active ingredient. Said agent is useful as a tonic or an antasthenic agent. Said agent is also useful by subjecting to oral administration as a drug or adding to various foods as a nourishing antasthenic food.

(Translation)

JAPANESE LAID-OPEN PUBLICATION NO. 3-44324

Laid-Open Publication Date: February 26, 1991
Title of the Invention: Sexual function invigorator
Application Number: 1-180867
Filing Date: July 13, 1989
Inventor: K. Tsuchiya
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Specification

1. Title of the Invention
Sexual function invigorator

2. Claim
1. A sexual function invigorator containing propentofylline or an intracorporeal metabolite thereof as an effective ingredient.

3. Detailed Description of the Invention
(i) Field of the Invention
The present invention relates to a sexual function invigorator containing propentofylline or an intracorporeal metabolite thereof as an effective ingredient.

(ii) Prior art and problems to be solved by the invention
It is a known fact that tea and coffee are popular in the world, and it has been found that theophylline and caffeine contained therein are important bioactive sub-

stances for their popularity. Recent studies have found that tea is effective in prevention of various diseases including fatty liver, cancer, diabetes and lipemia when taken continuously.

A substance having a sexual invigorating function effect has been demanded. However, detailed knowledge on functional aspects of sex, i.e., a neurophysical mechanism of generation of sexual desire, process of excitation and the like has not been obtained. In some people, the cerebrum plays an important role in such a mechanism, which makes it more difficult to find the mechanism.

The conventional studies have examined, in detail, the effects of sex hormones on the nerve and genital organs based on the process of the expression of sexual desire related to puberty. Voluminous results have been obtained. There is no doubt that many scientists consider the sexual function from the point of sex hormones.

However, the cerebrum (especially, limbic system and hypothalamus) is deeply involved in the sex-related problems of the middle-aged and elder people. Accordingly, the theory that hormones are involved is not effective or effective merely temporarily for the therapy of hypogonadism.

Based on experiments performed on monkeys, it is assumed that the main part of cerebrum which causes sexual desire or sexual acts is hypothalamus or limbic system. This is considered to be also applicable to the humans.

For example, it is known that an erection and other sexual acts are caused by stimulating the central part of the forebrain and hypothalamus in the vicinity thereof. It is reported that aphrodisia can be evoked by manipulating the amygdaloid nucleus, which is a part of the limbic system.

In view of these findings, development of a substance for mainly stimulating the central part of the cerebrum, especially, a substance for stimulating the hypothalamus or limbic system to invigorate the sexual function is demanded. So far, there has not been any such agent provided for general use, except for some narcotics.

(iii) Means for solving the problems

According to the present invention, a sexual function invigorator containing propentofylline or a metabolite thereof as an effective ingredient is provided.

Propentofylline is a xanthine derivative, and is 3-methyl-1-(5-oxohexyl)-7-propyl-7H-purine-2(3H),6(1H)-dione. Intracorporeal metabolites of propentofylline include a 5-hydrohexyl group (CH_3-CH(OH)-$(CH_2)_4$-), a 4-carboxybutyl group (HOOC-$(CH_2)_4$-), and a 3-carboxypropyl group (HOOC-$(CH_2)_3$-) obtained from a 5-oxohexyl group (CH_3-CO-$(CH_2)_4$-).

The active ingredient of the present invention is considered to act on an upper central part of the cerebrum although any proof directly connecting the active ingredient and the effect has not been obtained. Thus, the active ingredient of the present invention has a sexual invigorating function. Accordingly, this ingredient is useful as a

tonic (or an antasthenic).

Usually, oral administration is preferable. However, the active ingredient can be administered in a non-oral manner (injection into muscles or intravenous injection) after being suspended or dissolved in an appropriate medium. Alternatively, the active ingredient can be administered transdermally in the state of being contained in a tape. The amount for oral administration is 10 mg to 1800 mg per day. Preferably, an amount of 60 mg to 600 mg is administered once to several times a day. Administration on a regular basis after every meal is possible. In the case of oral administration, the active ingredient can be administered together with an excipient such as lactose or starch. Alternatively, the active ingredient can be administered together with various gastric mucosa protective agents (e.g., vitamin U, sucralfate, L-glutamin, azulene, gefarnate, urogastrone, aldioxa, extract of licorice, proglumide, sofalcon, and FM-100) in order to alleviate the stimulation on the stomach. Furthermore, the active ingredient can be administered with vitamins such as vitamin E and vitamin B, zinc, extract of ginseng, pollen, royal jelly, honey, lurong, epimedii herba, buguzhi, gejie, rehmanniae radix, or angelicae radix.

The active ingredient can also be added to various types of food to prepare nutritious antasthetic food.

When the invigorator is independently administered in a large amount (e.g., 200 to 600 mg), the sexual function invigorating effect is expressed within 1 to 8 hours, and

achieves the peak in 6 hours.

Propentofylline, which is the representative active ingredient of the present invention, have the following characteristics on toxicity, carcinogenicity, absorption and excretion.

1) Toxicity test (acute toxicity: LD_{50}, mg/Kg)

		Oral	Intravenous	Abdominal cavity	Subcutaneous
Mouse	♂	900	168	375	450
	♀	780	170	346	508
Rat	♂	1150	180	199	400
	♀	940	195	196	338

After propentofylline was administered to rats in an amount of 50 mg/Kg/day for 30 days (oral administration), no toxicity was exhibited.

After propentofylline was administered to dogs in an amount of 20 mg/Kg/day for 6 months, no specific change was exhibited.

2) Sexual reproduction and carcinogenicity tests

Experiments performed on mice exhibited no teratogenicity. Experiments performed on rats exhibited no carcinogenicity after 2-year observation.

3) Transmigration, cumulativity, absorption and excretion

Propentofylline has 5 to 7 times the lipid solubility than the conventional xanthine derivatives and thus can be absorbed satisfactorily through the cell membrane. Propentofylline is absorbed through skin and intestine. Propentofylline can pass blood-brain barrier and thus is considered to have a significant effect in the brain.

Repeated administration on rats did not exhibit cumulativity.

An oral administration test performed on dogs has shown that propentofylline appears in blood in 10 to 15 minutes, reaches the peak in the amount in 4 to 8 hours, and disappears from the blood 10 to 20 hour after that.

Within 24 hours after administration, about 90% of propentofylline is excreted in urine.

4) Propentofylline has been confirmed not to influence the introductory hours of sleep or the hours of sleep. Propentofylline has also been confirmed to have no influence on movement of digestive tract or secretion of gastric juice.

The clinical effects will be shown in order to demonstrate the effectiveness of the active ingredient of the present invention.

Test sample

1. 39 years of age, male

The subject's sexual desire had been withering for the previous 4 to 5 years. A sufficiently hard erection was not obtained. Morning erection had become less frequent. As a result of taking 100 mg of propentofylline after each meal, three times a day, all the above-mentioned symptoms were alleviated during the second week. However, since the subject had been taking zinc sulfide, pollen, vitamin E, ginseng and the like for the previous several months, it was not clear the effect was obtained only by propentofylline.

2. Ten males (35 to 50 years of age) who were healthy but felt some hypogonadism were given propentofylline for 2 months (after each meal, three times a day, 100 mg per dose, orally administered). After the test, the ten males answered a questionnaire.

a) Hypogonadism was alleviated: 7
b) Sexual feeling was improved: 3
c) Frequency and hardness of erection were improved: 2

One person felt an increased energy level, and one person experienced a more focused mental state. Among the people who experienced some effect, about 60% experienced the effect in a relatively short time (1 to 14 days). This shows that propentofylline is effective immediately. No side effects were found in any of the ten males.

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Counterpart U.S. Patent No. none